REMARKS

This Response is being submitted in response to the Office Action dated April 14, 2009. Claims 6, 13, 16, 18, 21, and 23 were previously cancelled, claims 2-5, 7-12, 14-15, 17, 19-20, 22, and 25-26 were previously amended, and claims 1 and 26 are hereby amended. No other claims are added, amended or cancelled. Claims 1-5, 7-12, 14-15, 17, 19-20, 22, and 24-26 are and remain pending in this application and claims 1-5, 7-12, 14-15, 17, 19-20, 22, and 24 and 26 stand finally rejected. Reconsideration and reexamination are respectfully requested. Claim 25 is allowed.

Withdrawn Rejections

Applicant notes with appreciation the withdrawal of previous objections to the specification and to claim 17, as well as the withdrawal of the previous rejections to claim 25 under section 112, and to claim 26 under section 103.

Response to Arguments and New Amendment/Arguments Pursuant to 37 CFR 1.114(c) and 1.111 (including In re Geiger, inter alia)

Applicant respectfully submits that the data provided supports the improved effects of the present composition alone as well as in view of EMLA. There is an obvious improvement regardless, and indeed because of the comparison using the different variables (time, amount of anesthetic components, length of application time, occlusion). Indeed, what the data shows is that over a period of less time and without occlusion, the composition of the present application is more effective than the known EMLA of the state of the art. This is sufficient effectiveness without necessity of a one-to-one showing.

The Office Action alleges that "to effectively demonstrate unexpected results, the variables . . . governing the results need to be compared side by side, and tested one variable at a time." (OA, page 4, lines 18-20.) However, this sets the bar much too high. Rather, the true standard for comparison goes all the way back to Graham v. John

Deere, 383 U.S. 1 (1966) which requires that the differences between the claimed subject matter and the state of the art be first determined and then evaluated by the person having ordinary skill in the art. And, indeed, this is a reasonableness standard, also referred to as a "preponderance of the evidence" standard; In re Glaug, 283 F.3d 1335, 1338 (Fed.Cir. 2002), when all evidence weighed together is simply more likely than not to demonstrate non-obviousness. I.e., what would a person of ordinary skill in the art have thought about the evidence? Would it more resasonably than not be understood by that person as indicating non-obviousness. In such a case, then, "[e]vidence that a compound is unexpectedly superior in one of a spectrum of common properties . . . can be enough to rebut a *prima facie* case of obviousness." No set number of examples of superiority is required. *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987), MPEP 716.02(a).

A similar prior case contains an excellent discussion of the law of comparative testing; see In re Geiger, 815 F.2d 686, 690, 2 USPQ2d 1276, 1279 (Fed. Cir. 1987) (J. Newman concurring). In particular, it is noted there that an applicant's showing of comparative data need only be "reasonable" to be sufficient, and that "the comparative showing 'must be sufficient to permit a conclusion respecting the relative effectiveness of applicant's claimed compounds and the compounds of the closest prior art,'" (quoting In re Payne, 606 F.2d 303, 316, 203 USPQ 245, 256 (CCPA 1979)). Note, the facts of Geiger involved an application for a three-component compound which the applicant had tested against known combinations of two components thereof; however, the Patent Office had rejected on the argument that the evidence was insufficient in that no data had been provided for one of the highly active ingredients alone because the Patent Office could not determine how much of the effectiveness was due to that ingredient alone. Such evidence was ultimately found not necessary by the Appellate Court because the two-component evidence already provided was "reasonable."

Indeed, Judge Newman went further noting that "[i]t is not required that the claimed invention be compared with subject matter that does not exist in the prior art. The applicant is not required to create prior art, nor to prove that his invention would

have been obvious if the prior art were different than it actually was." Id. See also In re Fenn, 639 F.2d 762, 765, 208 USPQ 470 (CCPA 1981) (prima facie obviousness may be rebutted by an *indirect* comparison of data which is of record).

Applied here, Applicant need only provide evidence sufficient for an ordinarily-skilled artisan to reasonably conclude superior results. There is no requirement for testing "side by side, and tested one variable at a time" as alleged in the OA, pg. 4, ll. 20. Thus, it is clear that an ordinarily-skilled artisan would very readily appreciate that the data in tables 1-3 of the specification show that the new three-component product here, lidocaine-prilocaine-tetracaine offers superior results in pain management and reduction of adverse effects; and it does so in less time and without the application of an occlusive dressing. There is no question of the superiority of these results and that they are reasonable as viewed by an ordinarily-skilled artisan.

Even so, Applicant further notes that the claimed compound is structurally distinct over the state of the art in that it includes the claimed feature of not needing occlusion. Applicant notes it as a distinguishing claimed feature over the prior art. Applicant thus respectfully submits not only that the present development presents a more effective anesthetic treatment for the reasons cited herein, but also with the structural distinction of doing so without necessity of occlusion. None of the cited prior art references teach, suggest, or motivate how to achieve this end.

Applicant further submits that these effects are present in all the claimed compositions, i.e. that they can be extrapolated reasonably by an ordinarily-skilled artisan, and by the law; see *In re Chupp,* above, and not only for the amount of anesthetic components of the specific formulation of claim 25. Finally, Applicant submits that there is a demonstrable synergistic effect in the decrease of side effects (see tables 2 and 3) with the three anesthetics as used together and as described in the application, compared to the 2-components combinations, and that prilocaine demonstrably stabilizes tetracaine. These conclusions are reasonable for an ordinarily-

skilled artisan using the data presented in the specification. Even so, Applicant addresses the rejections further below.

Rejections Under 35 U.S.C. § 103

Claims 1-5, 7-12, 24, and 26 continue to stand rejected under 35 USC 103(a) as purportedly being unpatentable over Cassel (US 2002/0128285, hereinafter "Cassel"), and, separately, that Claims 1-5, 7-9, 19-20, 22, 24, and 26 continue to stand rejected under 35 USC 103(a) as purportedly being unpatentable over Samuels et al. (US 2002/0006435 A1, hereinafter "Samuels"). Claims 14-15 continue to stand rejected as purportedly unpatentable over Cassel in view of Lutz et al. (US 5,750,139, hereinafter "Lutz"), and Claim 17 continues to stand rejected as purportedly unpatentable over Cassel in vies of Santana et al. (US 2003/0103955 A1, hereinafter "Santana").

Applicant's development is not obvious to one skilled in the art for the following reasons, as well as for the reasons as previously presented, inter alia. On this note; Applicant respectfully re-iterates and incorporates here by reference the comments made in his response of July 16, 2008 as if fully set forth here.

Even so, in summary, the presently claimed combination provides unpredictable purposes and unpredictable results, and is thus NOT a mere substitution or addition for a known purpose, nor yielding predictable results. Therefore, and per the Supreme Court case of KSR International Co. v. Teleflex Inc., 550 U.S. 398, 82 USPQ2d 1385 (2007), the present claims are thus patentable over the cited art.

The advantages of the presently claimed formulations are fully supported by the experimental data included in the present specification in Tables 1-3 wherein a greater efficacy is shown a shorter time of effect versus EMLA for the same type of dermatological and/or dermoesthetic procedure, and structurally without occlusion as claimed. The effectiveness of EMLA is practically half with a doubled time of application. This is/will be reasonably appreciated by an ordinarily-skilled artisan, and thus are the

kinds of unpredictable purposes and/or effects which support patentability under KSR, inter alia.

Prior art cited in the Office Action

Cassel

Cassel arguendo teaches "topical delivery of a local anaesthetic" and that "the preferred local anaesthetics include lidocaine, prilocaine, and tetracaine" as well as a lidocaine/prilocaine composition and a lidocaine/tetracaine composition. However, Cassel does not teach a three component composition as here; and as introduced above and described further below, Applicant's composition provides one or more new and different, unpredictable purposes, not the "same purpose" and thus it would NOT have been obvious to one ordinary skill in the art at the time of the invention" to combine to achieve the three component composition.

Note of the Cassel developments, the first combination lidocaine/prilocaine was sold as EMLA and the second lidocaine/tetracaine was known as AMLI cream. Cassel does not teach anything more than the prior existence of these two commercial formulations and his adoption for use in his process. However, as known, EMLA presents some adverse effects, so in Applicant's' Background section it is disclosed that there have been several attempts trying to improve EMLA cream (including provision of a vasodilator, or a lipophilic base) (see Bouffard Fita specification, para. [0011]). The data of Tables 1-3 show superior results over EMLA and are thus non-obvious thereover.

Moreover, merely combining known prior art elements is not sufficient to render the claimed invention obvious if the results would not have been predictable to one of ordinary skill in the art. KSR International Co. v. Teleflex Inc., 550 U.S. 398, 82 USPQ2d 1385 (2007). There is no indication that such superiority of results is predictable from Cassel, or any other art. Thus, the present claimed compositions are not obvious thereover.

Furthermore, there is no motivation to make the present combination merely because each of the prior art compositions have separate, discrete utilities as topical anesthetic compositions. Indeed, there is neither teaching in Cassel nor motivation therefrom to combine both compositions to get a new composition, particularly not a new composition with the unpredictable different and new purposes, effects and utilities of the presently-claimed new compositions; the purposes/effects namely being, the removal of the previously compulsory occlusion; the reduction in side effects; the speeding of the anesthetic effect; the lengthening of the anesthetic effect; and the increase in tetracaine stability, bioavailability and, therefore, anesthetic effect, due to the presence of prilocaine. No such prior utilities, purposes or effects existed and thus no such motivation exists to create them.

Thus, what is provided here is not a mere substitution or even addition of parts for the same purpose, but rather an addition to achieve one or more additional purposes hitherto unknown nor predicted, at levels and speeds unsuggested, not taught and not motivated by the art. KSR said substitution for the same purpose may not be patentable; however, here we have addition for one or more different purposes, heretofore unpredicted.

From the points set out above, the obviousness rejection on Cassel is obviated and/or traversed. Thus, Applicant's Claim 1 is not obvious from Cassel. Moreover, Applicant respectfully submits that Applicant's dependent claims 2-5, 7-12, and 24, are allowable at least, for the same reasons set forth above in that they contain the combination of elements of claim 1 which are not properly taught or suggested by Cassel. Claim 26 is likewise patentable over Cassel. Reconsideration and withdrawal of these rejections are thus also respectfully requested.

Samuels

Samuels arguendo teaches "compositions for topical application comprising a therapeutically effective amount of topical anesthetic" and that "preferred agents include

lidocaine, prilocaine, and tetracaine" and further combinations of lidocaine/prilocaine and lidocaine/tetracaine. However, it would not be obvious to one skilled in the art to determine the optimal or workable amount of the Applicant's components, which are not found in Samuels. As introduced above, and described further below; Applicant's composition provides one or more new and different, unpredictable purposes, not the "same purpose."

The reasons are substantially the same as those argued above with respect to Cassel: in Samuels, a different problem is solved, and the composition here is set forth not for the same purpose, but, for the accomplishment of one or more of multiple different and new, as-yet unpredicted purposes. The skilled in the art would have not been motivated because the problem(s) to be solved by Applicant is(are) different one(s) from the mere providing of "a composition with utility as topical anesthetic composition". Applicant's problem to be solved is/was not merely providing another topical anesthetic composition. Rather, the problem to be solved is/was to provide a topical anesthetic composition that overcomes the problems of EMLA and others. Samuels certainly does not teach that modifying the composition by adding a new anaesthetic component would result in any improvement in any aspect. In Samuels, combinations of two and three anesthetics are mentioned, but there is not any indication that by adding a further anasthetic component any improvement is achieved.

The problem to be solved in Samuels was to achieve a prolongation of anesthesia by the incorporation of a non-anasthetic component, particularly there, a vasodilator, into the composition including transdermal anesthetics and a carrier. As noted below, this Samuels direction actually teaches away from addition of a third anaesthetic; Samuels is teaching a vasodilator to lengthen effect, hence giving up on the field of anasthetics alone to lengthen effective time. Samuels in effect teaches others that if they want longer activity they need to go to a very different kind of additive, the vasodilator, teaching away from adding a third anaesthetic.

Therefore, there is no motivation neither teaching derived from Samuels to combine the two combinations lidocaine/prilocaine and lidocaine/tetracaine in order to get the new three-component composition of Applicant with the new and different and as-yet unpredictable results here achieved. The composition of Applicant is another very different and independent solution to the different problem of improving properties of anesthetic compositions.

Thus, Applicant's claim 1 is not obvious from Samuels. Moreover, Applicant submits that Applicant's dependent claims 2-5, 7-9, 19-20, 22, and 24, are allowable at least, for the same reasons set forth above in that they contain the elements of claim 1 not properly taught or suggested by Samuels. Claim 26 is likewise patentable over Samuels. Reconsideration and withdrawal of these rejections are thus also respectfully requested.

Cassel and Lutz

First of all, Lutz does not cure the lacking of Cassel in not disclosing or suggesting the combination of all three anasthetics herein issue. Thus, no combination of Cassel with Lutz will result in any of the claimed compositions and thus, such combination Cassel with Lutz fails to render obvious Applicant's independent and dependent claims having such elements. Claim 14 and 15 are thus patentable over Cassel in view of Lutz.

Moreover, the Office Action recognizes that Cassel does not teach dimethyl sulfoxide nor its amounts present in the composition as a penetration enhancer as presently claimed in Claims 14-15.

As a further matter, Lutz is directed to benzopyrone and the dermal application thereof. Benzopyrone is used for venous, vascular diseases, protein-rich edemas, and protein-rich lymphedemas, particularly for chronic venous insufficiency, phlebitis, and cancers. This is non-analogous art to that practiced by Applicant and described in Applicant's specification.

Furthermore, both Cassel and Lutz are complete inventions in and of themselves. The skilled artisan in Cassel would not look to Lutz to solve a problem already solved by Cassel, and vice-versa.

As explained above, the amount of experimentation necessary to reach the desired amounts would be beyond that undertaken in either Cassel or Lutz. This further illustrates the nonobviousness in Applicant's development.

Additionally, Lutz requires at least one neutral or carboxylic acid-based active ingredient, which Applicant does not. Finally, Lutz mentions in passing that DMSO and N-methylpyrrolidone can be used as a solvent. As conceded in the Office Action, Lutz does not teach any amounts.

Thus, claims 14-15 are not obvious on any combination of Cassel and Lutz.

Cassel and Santana

First of all, Santana does not cure the lacking of Cassel in not disclosing or suggesting the combination of all three anasthetics herein issue. Thus, no combination of Cassel with Santana will result in any of the claimed compositions and thus, such combination Cassel with Santana fails to render obvious Applicant's independent and dependent claims having such elements. Claim 17 is thus patentable over Cassel in view of Santana.

Moreover, the Office Action recognizes that Cassel does not teach hyaluronidases or derivatives of mucopolysaccharides as a spreading agent as presently claimed in Claim 17.

As a further matter, Santana does not teach mucopolysaccharides in general, as does Applicant, but is instead limited to hyaluronidases. Furthermore, Santana teaches hyaluronidase as part of a specific three-element composition of diclofenac. Diclofenac has an anti-inflammatory effect and is used, i.e., to treat arthritis. This is non-analogous art to that practiced by Applicant and described in Applicant's specification.

Furthermore, both Santana and Cassel are complete inventions in and of themselves. The skilled artisan in Cassel would not look to Santana to solve problem already solved by Cassel, and vice-versa.

As explained above, the amount of experimentation necessary to reach the desired amounts would be beyond that undertaken in either Cassel or Santana. This further illustrates the nonobviousness in Applicant's development.

Finally, Applicant's situation is not analogous to simply 'reading a list and selecting a known compound to meet known requirements'. Applicant conducted experimentation and balancing to determine proper amounts despite indications to the contrary set forth in the prior art. Therefore, Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327 (1945), is inapposite. The situation here has little to do with simply fitting the last piece into a jigsaw puzzle. There are no 'pieces' provided by Cassel and Santana, the latter of which fails to teach the mucopolysaccharidases discussed in Claim 17. The situation would be more analogous to someone having to machine their own jigsaw puzzle piece, which is far beyond the principles of Sinclair & Carroll, supra,.

All of the obviousness rejections are thus obviated and/or traversed and can be withdrawn. Action to this end is respectfully requested.

Rejections Under 35 U.S.C. § 112

Claim 26 stands rejected under section 112, second paragraph as allegedly indefinite.

Applicant disagrees with the assertion of indefiniteness; however, has amended claim 26 herein and this rejection is thus moot. Withdrawal is respectfully requested.

Allowable Subject Matter

Applicant notes that Claim 25 has and is directed to allowable subject matter.

CONCLUSION

Applicant notes that all rejections are obviated or traversed and respectfully requests that they thus be withdrawn. A timely Notice of Allowance is thus requested to be issued in this case. Applicant believes that other than the RCE fee and the extension of time fees, no other fees or petitions are due with this filing. However, should any such fees or petitions be required, please consider this a request therefore and authorization to charge Deposit Account No. 02-2093 as necessary.

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Respectfully submitted,

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